

REMARKS***Concerning 35 USC § 112, first paragraph***

Claims 37-52 of record stand rejected pursuant to 35 USC § 112, first paragraph, as lacking enablement for the airway response and route of administration recited in the claims.

Applicant's representative, S. Serge Shahinian, thanks Examiner Nolan for the opportunity to discuss these rejections in a personal interview on June 24, 2003.

Examiner Nolan objected to the expression "stimulus-induced airway response" in claim 37 on the assertion that it reads on "epinephrine induced bronchial relaxation," which the Examiner considers would not benefit from treatment with CGRP. The Examiner agreed that this objection would be obviated if claim 37 were to be amended to recite the Markush group of airway responses formerly recited in claim 40. Therefore, without acquiescing with the rejection, and solely to advance prosecution, claim 37 has been amended to recite that the stimulus-induced airway response is selected from the group consisting of airway constriction, bronchospasm, airway hyperreactivity, eosinophil accumulation in bronchial walls, an increase in airway resistance, or combinations thereof. Claim 40 has accordingly been cancelled.

Regarding the recited route of administration, Examiner Nolan contended that the specification provides support only for administration of CGRP by inhalation. Applicant respectfully disagrees, as the effectiveness of CGRP in this regard is clearly shown in the examples to function via various routes of administration, including intravenous administration (see Example 2) as well as inhalation (see Examples 3 and 4). However, solely to advance prosecution, claim 37 has been amended to recite that the agent is administered by inhalation. Claims 47 and 48 have accordingly been cancelled. Applicant reserves the right to pursue any subject matter removed by such amendments in one or more continuation applications.

Other issues

During the above-mentioned interview, Examiner Nolan requested clarification of the definition of the term "CGRP," based on his understanding of the definition of this term on page 17 of the specification. In response, applicant respectfully submits that the terms "human CGRP" and "rat CGRP" encompass any naturally-occurring form of CGRP found in human or rat, respectively. These include, for example, the α and β forms of human and rat CGRP, which are described in Zaidi *et al.*, *Critical Reviews in Clinical Laboratory Sciences* 28: 109-74 (1990), a copy of which accompanied Applicant's letter of November 14, 2001 (see Table 3 on page 119, where "1" and "2" denote the α and β forms, respectively). Examples of known human and rat CGRP peptides within the scope of the present claims are also shown in for example the Sigma-Aldrich catalogue (excerpt attached).

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, he is invited to contact S. Serge Shahinian (Reg. No. 52,533) at 514-954-1500. Applicant respectfully requests the issuance of a Notice of Allowance in this case. Further, if the Examiner does not consider that the application is in a form for allowance, an interview with the Examiner is respectfully requested.

Respectfully submitted,

August 18, 2003

Date



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BIOACTIVE PEPTIDES

MISCELLANEOUS PEPTIDES

S Cdn
5 mg 106.70

n Lett., 2167

it., 4255

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10 µg 264.20
1 mg 472.10

Gly-Leu-Gly-Cys-

phys. Res. Com-

500 µg 243.20

Asp-Arg-Ile-Gly-
Leu-Arg-Arg-Tyr)

phys. Res. Com-

10 µg 252.10
1 mg 462.30

-Leu-Gly-Cys-

phys. Res. Com-

PRODUCT NUMBER	S Cdn	PRODUCT NUMBER	S Cdn
BRAIN NATRIURETIC PEPTIDE-45 100 µg 141.20		CALCISEPTINE 1 vial 534.40	
B 6154 Rat [C-0°C] (BNP-45; Ser-Gln-Asp-Ser-Ala-Phe-Arg-Ile-Gln-Glu-Arg- Leu-Arg-Asn-Ser-Lys-Met-Ala-His-Ser-Ser-Ser-Cys-Phe- Gly-Gln-Lys-Ile-Asp-Arg-Ile-Gly-Ala-Val-Ser-Arg-Leu-Gly- Cys-Asp-Gly-Leu-Arg-Leu-Phe) [Disulfide Bridge: 23-39] Minimum 97% (HPLC) Storage form of BNP-32 Ref.: 1. Aburaya, M., et al., Biochem. Biophys. Res. Commun., 163 , 226 (1989). 2. Kambayashi, Y., et al., Biochem. Biophys. Res. Commun., 163 , 233 (1989). [123337-89-3] FW 5040.7		C 1836 (Arg-Ile-Cys-Tyr-Ile-His-Lys-Ala-Ser- Leu-Pro-Arg-Ala-Thr-Lys-Thr-Cys-Val-Glu-Asn-Thr-Cys- Tyr-Lys-Met-Phe-Ile-Arg-Thr-Gln-Arg-Glu-Tyr-Ile-Ser-Glu- Arg-Gly-Cys-Gly-Cys-Pro-Thr-Ala-Met-Trp-Pro-Tyr-Gln- Thr-Glu-Cys-Cys-Lys-Gly-Asp-Arg-Cys-Asn-Lys) [Disulfide Bridges: 3-22, 17-39, 41-52, 53-58] From Black mamba (Dendroaspis polylepis polylepis) Minimum 97% (HPLC) Peptide content: Approx. 65% L-type Ca ⁺⁺ channel blocker. Vial contains 100 µg. Ref.: 1. Weille, J.R. De., et al., Proc. Natl. Acad. Sci., USA, 88 , 2437 (1991). 2. Kuroda, H., et al., Pept. Res., 5 , 265 (1992). [178805-91-9] FW 7036.1	
BRAIN NATRIURETIC PEPTIDE 100 µg 73.90		CALCITONIN GENE RELATED PEPTIDE (α-CGRP; CGRP-II) Potent, long-lasting vasodilator; activation of CGRP receptors on pancreatic β-cells increases plasma levels of pancreatic enzymes	
B 0777 FRAGMENT 7-32 [C-0°C] (BNP-26) Porcine Minimum 97% (HPLC) Peptide content: Approx. 65% Useful as an immunogen for preparing anti-BNP antibodies Ref.: Sudon, T., et al., Nature, 332 , 78 (1988). [114547-28-3] FW 2869.3		C 0167 Human [C-0°C] (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val- Thr-His-Arg-Leu-Ala-Gly-Leu-Leu- Ser-Arg-Ser-Gly-Gly-Val-Val-Lys- Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe- NH ₂) [Disulfide Bridge: 2-7] Minimum 95% (HPLC) [90954-53-3] FW 3789.3	100 µg 99.90 250 µg 218.80 500 µg 366.90
BUCCALIN 1 mg 41.70		C 0292 Rat [C-0°C] (Ser-Cys-Asn-Thr-Ala-Thr-Cys-Val- Thr-His-Arg-Leu-Ala-Gly-Leu-Leu- Ser-Arg-Ser-Gly-Gly-Val-Val-Lys- Asp-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Glu-Ala-Phe- NH ₂) [Disulfide Bridge: 2-7] Minimum 97% (HPLC) [96827-03-1] FW 3806.3	100 µg 105.20 250 µg 230.30 500 µg 386.20
B 4528 (Gly-Met-Asp-Ser-Leu-Ala-Phe-Ser-Gly- Gly-Leu-NH ₂) [C-0°C] Minimum 97% (HPLC) Ref.: Cooper, E.C., et al., Proc. Natl. Acad. Sci. USA, 85 , 6177 (1988). [116844-51-0] FW 1053.2		CALCITONIN GENE RELATED 100 µg 58.50	
BUFORIN I 500 µg 216.10		C 2806 PEPTIDE, Fragment 8-37 [C-0°C] Human (α-CGRP 8-37; Val-Thr-His-Arg- Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys- Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe- NH ₂) Minimum 97% (HPLC) Peptide content: Approx. 70% Selective competitive antagonist at CGRP receptors but not at calcitonin receptors Ref.: Chiba, T., et al., Amer. J. Physiol., 256 , E331 (1989). [119911-68-1] FW 3125.6	500 µg 194.30 1 mg 339.90
B 6173 (Ala-Gly-Arg-Gly-Lys-Gln-Gly-Gly- Lys-Val-Arg-Ala-Lys-Ala-Lys-Thr-Arg-Ser-Ser-Arg-Ala- Gly-Leu-Gln-Phe-Pro-Val-Gly-Arg-Val-His-Arg-Leu-Leu- Arg-Lys-Gly-Asn-Tyr) [C-0°C] Minimum 90% (HPLC) Peptide Content: Approx. 60% Antimicrobial peptide Ref.: Park, Chan Bae, et al., Biochem. Biophys. Res. Commun., 518 , 408 (1996). [173010-28-1] FW 4263.0		β-CALCITONIN GENE RELATED 100 µg 101.40	
BUFORIN II 500 µg 158.60		C 1044 PEPTIDE [C-0°C] Human (β-CGRP; CGRP-II; Ala-Cys-Asn-Thr-Ala-Thr-Cys-Val-Thr- His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Met- Val-Lys-Ser-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys- Ala-Phe-NH ₂) [Disulfide Bridge: 2-7] Minimum 97% (HPLC) Peptide content: Approx. 70% Potent hypotensive agent and vasodilator Ref.: 1. Steenburgh, P.H., et al., FEBS Lett., 183 , 403 (1985). 2. ibid., 209 , 97 (1986). [98824-26-1] FW 3793.4	1 mg 506.20
B 6298 (Thr-Arg-Ser-Ser-Arg-Ala-Gly-Leu- Gln-Phe-Pro-Val-Gly-Arg-Val-His-Arg-Leu-Leu-Arg-Lys) [C-0°C] Minimum 97% (HPLC) Peptide Content: Approx. 60% Antimicrobial peptide Ref.: Park, Chan Bae, et al., Biochem. Biophys. Res. Commun., 518 , 408 (1996). [172998-24-2] FW 2434.9			
BURSIN 5 mg 41.40			
B 5644 (Lys-His-Gly-NH ₂) [C-0°C] Trihydrochloride Minimum 97% (HPLC) Peptide content: Approx. 60% Ref.: Audhya, A., Science, 231 , 997 (1986). [112898-17-6] C ₁₄ H ₂₅ N ₇ O ₃ • 3HCl FW 448.8			
C3d PEPTIDE P16 100 µg 70.10			
C 1457 (Lys-Asn-Arg-Trp-Glu-Asp-Pro-Gly- Lys-Gln-Leu-Tyr-Asn-Val-Glu-Ala) [C-0°C] Minimum 97% (HPLC) Induces tyrosine phosphorylation of phospho- proteins 100 and 105 and in vitro proliferation of human B lymphocytes. Ref.: Frade, R., et al., Biochem. Biophys. Res. Com- mun., 188 , 833 (1992). [99027-06-2] FW 1947.1	500 µg 233.60		